dition; for we have all kinds of pressure conditions. We may have a high pressure with everything favorable, upon this supposition, for the development of pneumonia and right in the middle of it the opposing condition will occur. How can you correlate such conditions? From the standpoint of the climatologist I think that too much importance may be given to climate. It is a double-barreled proposition. You have climate and you have man. You must remember that one man will get pneumonia because of imprudent exposure and the other man, properly housed and cared for, will not have pneumonia. There you have climate control. In Chicago you may have the same climate, the same pressure say, yet the houses may be warm, and a man stepping out of his house may walk in slushy streets, or get into an environment favorable for pneumonia. I wish to pay tribute to the work Dr. Richter has done. This is in many ways a memorable paper. It opens up a wide field of investigation. He traces a relationship between pneumonia mortality and high pressure conditions that seems to be more than an accidental relation. He has done the work with great detail and with great labor, trying to trace the relationship between the demonstrated high air pressure condition and the prevalence of pneumonia. Dr. Richter has done a great deal of thoughtful and honest work and has opened up an important line of investigation for the medico-climatologist.

Dr. Richter (closing): This chart, exhibiting epidemics in Chicago and San Francisco during 5 years, I thought would interest you, first, because we practitioners have been taught that pneumonia is a disease, more or less under the influence of low temperature, that it spreads itself generally over the cold season of the year and that it is an infectious disease, which calls for a certain prophylaxis in regard to sputum. On this chart you find that, although pneumonia is more prevalent during the cold season, it appears in the form of epidemics of different magnitude in the different years, seasons and cities, and is entirely independent of low temperature, as the conditions in San Francisco exemplify. Secondly, we learn from this chart that these epidemics are a function of the prevalence of anticyclonic weather and I tried to lay all possible stress on the proposition to look for an explanation not in the mechanical pressure of the atmosphere, but in possible qualities of the air, as carried to us during an anticyclone from the higher levels. Such air should be supposed to be qualified by the radiant energy of the sun and to a different degree during the different periods of the sun's activity.

REVIEW OF RECENT WORK ON TUBERCULOSIS.*

By LEWIS SAYRE MACE, M. D., San Francisco.

The purpose of this paper is briefly to report some of the most important articles, which have appeared during the past year upon the subject of tuberculosis. No attempt has been made to report them all for that would clearly be impossible, but a resume of the work which has been done along the lines of etiology and diagnosis should serve to show the trend of modern experimental research in the field and to point the way to a better understanding of modern treatment.

Under the heading of etiology the statement of Koch, made before the London International Congress of 1901, that the human species was not subject to infection by the bacillus causing bovine tuberculosis takes first place in importance and interest. To settle this question a royal commission was appointed consisting of Sir Michael Foster, Woodhead, Martin, McFadyn and Boyce, whose second interim report (1) published in February, 1907, gives the results of their labors to this time. While their work is not by any means completed, it is evident from this report that their experiments are being made in the most thorough and scientific manner, and it is already quite apparent at what conclusion they will eventually arrive.

Their experiments with bovine tubercle bacilli were performed upon guinea pigs, dogs, cats, rabbits, goats, apes, baboons and monkeys, and the organism was found to be fatal to all these animals as well as to the bovine species and to act upon them in the main with neither more nor less virulence.

The human bacilli worked with fall into three groups. Group I resembles the bovine type in cultural characteristics and virulence upon the animals mentioned. They grow with difficulty upon artificial media as the bacilli of the bovine group do. After an injection of equal doses the animals used develop rapidly fatal general tuberculosis equally with those infected with the bacilli of the bovine group. In other words, Group I is the bovine bacillus and nothing else.

Group II are far less virulent to animals in the doses used than those of Group I. They grow easily upon artificial media. In comparatively large doses a rapidly fatal general tuberculosis does not follow in dogs, cats, guinea pigs, etc., while, on the other hand, when monkeys, apes and baboons are used a comparatively small dose is followed by rapidly fatal effect. The important fact is thus shown that their virulence increases as the animals used approach the human type.

Group III is intermediate in virulence between Group I and Group II. It lies between the two in cultural characteristics, and it is generally unstable and variable in its virulence.

In conclusion, the committee say: "Of the sixty cases of the human tubercle bacilli studied by us fourteen belong to Group I, that is to say, contained the tubercle bacilli of the bovine type. Of these sixty cases twenty-eight possessed clinical histories indicating that in them the bacillus was introduced through the alimentary canal. Of these, thirteen belonged to Group I. Of the nine cases in which cervical glands were studied by us 3, and of the nineteen cases in which lesions of abdominal tuberculosis were studied by us, 10 belonged to Group I. These figures indicate that a large per cent of tuberculosis contracted by ingestion is due to the bovine

* Read before the Cooper College Science Club, March, 1908.

bacillus. A very considerable amount of disease and loss of life must be attributed to the use of cows' milk containing tubercle bacilli, and such milk ought never to be used as food. Our results clearly point to the necessity of measures more stringent than those at present enforced being taken to prevent the sale or consumption of such milk."

The question whether heredity or contact infection is the more important factor in human tuberculosis is well discussed by Hazen (2) of Johns Hopkins. At the Phipps Dispensary, he says, they believe heredity to play a minor role. For this paper eighty-three families were studied containing five hundred and thirty-four individuals, of whom two hundred and fifty-four were tuberculous, thirteen suspicious, and two hundred and sixty-seven well. These figures alone speak for contact infection. Sixty-two of the patients were free from hereditary taint, and his careful analysis of the statistics at hand certainly speak for the importance of contact infection. Of forty-eight individuals exposed by marriage, twenty-one have contracted the disease and two are suspicious. Where the husband or wife had tuberculosis the other developed it in 43% of the cases. In fifteen instances, one or both parents suffer from tuberculosis and the children are free. And the most striking fact of all is that out of two hundred and fifty-four patients, only three who were not in contact, developed the disease.

All of this would tend to show that more or less intimate contact with the tubercular is a prime factor in the dissemination of the disease and that any hereditary taint can be ignored. Nevertheless, the fact so long observed clinically that children of tuberculous ancestry in many cases show lack of resistance to the disease cannot be denied. Although some writers go so far as to refuse to acknowledge the possibility of any hereditary tendency to tuberculosis, the fact that it does exist cannot be seriously questioned. In this connection, the work of Vaughn and Wheeler (3) on the production of anaphylaxis or hypersusceptibility to albumen injections should be mentioned in that their experiments showed that this specific hypersusceptibility was transmitted through the mother to her offspring. And certainly if anaphylaxis, which is a condition in which the cell body has developed to a high degree the power of elaborating a proteid splitting enzyme like body, is transmissible to offspring, it should hardly be a cause for doubt that the susceptibility to tuberculosis should be transmissible also.

To make this point clearer I should speak further of this condition of anaphylaxis or hypersusceptibility. The authors quoted have been working upon the separation of a poison group in the proteid molecule of egg-white. Following the previous work of Rosenau and Andersen[6] they established a condition of anaphylaxis against this proteid to prove that their separation of poison group and nonpoison residue was an actual one. One injection of egg-white they found to be without effect, while a second likewise was ineffective if made within a few days after the first. If ten or twelve days, however, were allowed to elapse, the second injection caused poison symptoms consisting of: 1st. Evidences of peripheral irritation, violent scratching, etc.; 2d. Paralysis, especially of the hind legs; and, 3d, Violent clonic convulsions and death from respiratory failure. This corresponds to what has long been known to occur while using guinea pigs for standardizing diphtheria antitoxin. These animals would often die suddenly without known cause following subsequent injections of horse serum upon whom the first had had no effect. Vaughn and Wheeler explain this as due to a condition of hypersusceptibility developed in the following way: The first injection of proteid is slowly split up as the body cells are unprepared with the binding group or enzyme-like body in any large quantity. The toxiphore or poison group is therefore released but slowly, and is eliminated without doing harm. In the process, however, the cells have acquired the ability to elaborate the binding group or receptor group in large quantity, and a second dose of proteid is rapidly split up and the poison group is liberated, causing its symptoms depending upon the dose used. The fact that this condition of anaphylaxis is transmitted by the mother to offspring should be considered before denying the possibility of the inheritance of susceptibility or loss of resistance to tubercular infection.

Some very valuable work has been done along lines suggested by Von Behring's theory that practically all tuberculosis is intestinal in origin and transmitted in infancy by means of cows' milk or swallowed particles of dust and dirt. The fact that tubercle bacilli may gain admission to the lymph stream through the intestinal walls without infecting them in transit or loosing their virulence is well established. Schlossman and Engle[4] injected an emulsion of tubercle bacilli into the stomach of guinea pigs after laparectomy. The experiment was carried out with great care and attention to detail to prevent the accidental infection of the blood during the operation. A few hours after the operation the bacilli were constantly found in the lungs, having gained admission to the mesenteric lymph vessels, thence to the thoracic duct and from this to the right heart and lungs. In the same line with these researches is the experimental anthracosis after the theory of Calmette that this disease is always of intestinal origin. Van Steenburg and Sommerville[5] adhere to their previous statement that it is possible for coal dust to traverse the wall of the intestine and reach the bronchial glands and even the lungs themselves. Corroborating these experiments is the work of Petit[7] and Vallee[8] and others, and while many workers do not agree and are unwilling to believe that the lungs can be infected by tubercle bacilli through the blood in the manner stated, still it must be confessed that the evidence at hand seems to show that it is possible and more than probable that in a vast majority of cases tuberculosis has its origin in ingested rather than inhaled infectious material. This should be taken as an added proof if any were needed that all tuber-

culous milk should be excluded from the infants' dietary.

The recent work on the early diagnosis of tuberculosis may well be introduced by consideration of the paper by Hamman and Wolman[9] of Johns Hopkins, since it deals principally with physical diagnosis and tends to show that entire attention of late has not been devoted to serum reactions. The question "How marked must the signs be in order to pronounce a suspect to be a tubercular" is answered by the consideration of one hundred and fifty early cases received at the Phipps Dispensary, all of which were proved subsequently to be tubercular by the finding of tubercle bacilli or a positive tuberculin reaction or the subsequent development of the case. All showed one or all of the three cardinal signs, alteration of the percussion note, modified breath sounds and rales. Where these three signs occur together, no matter how slightly marked one or another may be, the case is unhesitatingly pronounced tuberculosis. In sixty-one patients of this group the three signs did not occur together and hence the physical diagnosis alone was not sufficient for diagnosis.

In 29, or 47%, change in percussion note was present. Rales were present in 53% and modified breath sounds in 61%. Modified breath sounds is therefore the most frequent early sign. Where only one sign of the three was present rales was slightly in the lead. In 2-3 of the group two signs were present; they were, percussion note and rales 16%. Breath sounds and rales in 23% and percussion note and breath sounds in 25%. Alteration of breath sounds being decidedly in the lead.

In 60% of these cases the respiratory rate was above 20 per minute; and 42% of these complained of loss of weight, half of these knowing of no disturbance of digestion or appetite to account for this loss. On account of these being ambulatory patients no temperature record was obtainable, otherwise the number of positive diagnoses from signs and symptoms might have been much larger.

It is interesting to note that 60% of the early cases were diagnosticated from physical examination alone, leaving but 40% in which further evidence was necessary for positive diagnosis.

In considering the diagnostic and therapeutic uses of tuberculin as affected by recent researches it seems important to review some of the investigations into the cause of the tuberculin reaction and recent rpogress into the study of tuberculin immunity, especially so since these studies have already resulted in the better understanding of the use of tuberculin as a remedy and have led to a wide appreciation of its value.

On the injection into the circulation of a foreign proteid, such as horse serum, egg-white or bacterial bodies, certain profound changes occur in the body cells as a result of which they acquire the ability to split up rapidly a succeeding dose of the same proteid. This is the reaction of anaphylaxis, which plays a most important part in the production of active immunity. In the case of the subject infected with tuberculosis the cells have already been rendered hypersensitive by the action of the invading organism, and the injection of tuberculin is therefore followed by the rapid splitting of this substance into its poison and non-poison groups. Binding of the toxophore group by the sensitized cells occurs, followed by the typical reaction. In the nontuberculous, on the other hand, where this condition of anaphylaxis does not exist, the cells, lacking the necessary binding group, can produce it but slowly. Consequently, the poison is liberated slowly and eliminated rapidly without causing the poison symptoms, which constitute the tuberculin reaction. It is therefore necessary to bear these facts in mind and to give as small doses as possible, repeated no oftener than necessary to give the characteristic reaction. Roth-Schultz[11] prefers to begin with .5 mg. doses increasing slowly to 2.5 mg. Roepke[12] advocates rapidly advancing to 5 mg. doses, which is half the maximum dose of Koch. This rapid increase of dosage appears the more rational method since we should remember that anaphylaxis may be induced by small doses of tuberculin, provided sufficient time is allowed to elapse between injections.

Wasserman[13] and his pupils have carried the investigations still further, and have elaborated an interesting theory of the cause of the tuberculin reaction. According to Wasserman, the condition of hypersensitiveness is the first stage in the production of active immunity. That is to say, the cells in proximity to the tuberculous lesion are well supplied with amboceptor groups. These seize upon and bind the invading proteid by means of one affinity, and by means of the other bind the complement constantly present in the serum. This latter body, by means of its ferment action, acts upon the cells, causing the softening and disintegrating of these tissues accompanied by the general symptoms of fever, etc. However this may be, and the ferment action of bound complement may well be questioned, his results are important since they demonstrate that the antibody to tuberculin, in other words, anti-tuberculin or amboceptor group, is formed by the cells under the influence of tuberculin treatment and can be demonstrated in the serum with more or less regularity.

The method Wasserman has used to prove the presence of this antibody is that known as fixation of complement, which is briefly as follows: The serum of an animal is rendered immune to the red blood cells of another species. In this manner, one obtains a serum, which, by means of its amboceptor group, will unite with these red cells on one hand, and on the other will unite with and bind the complement necessary for the hæmolysis. The amboceptor is not rendered inactive by heat while the complement is thermolabile; thus it is easy to differentiate one from the other and to show the presence of the immune body.

Thus: If to a serum of a tubercular subject containing tuberculin antibodies a suspension of tubercle bacilli is added presumably will follow a union of bacilli, amboceptor and complement. Now, if to this mixture is added an inactivated im-

mune serum plus an emulsion of the foreign red blood cells, no haemolysis will follow since the complement necessary has been found by the tuberculin antibody. But if the specific antibody were not present in the suspected serum the complement would not of course be bound, and upon the addition of the haemolytic system haemolysis would follow.

The results of these investigations show very conclusively that as a rule no free antibody is present in the serum of tuberculous subjects, but that it can be found fairly regularly in the serum of such patients when treated with tuberculin for a sufficient length of time.

Citron [14], in an exhaustive article on the causes of the tuberculin reaction, differs somewhat from Wasserman in that in common with Weil and others he questions the ability of bound complement to exert its digestive action.

In following the results of tuberculin therapy over long intervals of time he concludes that the reaction of anaphylaxis is the precursor of the active immunity induced by this method. He divides the course into four stages: First, increase of fixed cell receptors corresponding to the stage of hypersensibility. Second, increase of fixed cell receptors and beginning stage of free antibodies in the blood. Third, great numbers of fixed cell receptors and dimunition of free antibodies. Fourth, after long continued injection of tuberculin, anti-tuberculin is found in the blood, together with great numbers of fixed cell receptors and free antibodies at point of local infection.

The practical application of this is as follows: To produce active immunity in tuberculosis, tuberculin must be injected over a long period of time beginning with very small doses, 1/1000 mg. old tuberculin or 1/10,000 mg. T. R., according to Trudean [15], and increasing gradually to many thousand times the original dose, taking great care in the meantime to watch for the minor symptoms of headache, nausea, temperature rise, etc., which, though insignificant in themselves, may show that the limit of toleration has been reached and that the dose must be reduced or omitted until it shall be safe to begin again the gradually increasing doses.

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2. Home Factor in Tuberculosis. Hazen. Johns Hopkins Hospital. Bulletin Aug., 1907, p. 298.
3. Effect of Eggwhite and Its Split Product on Animals. Journal of Infectious Diseases, June 15, 1907, p. 476. Vaughn and Wheeler.
4. Zur Frage der Eutstehung der Lungen Tuberculose. Schlossman and Engel. Deutsch, Med. Woch., 1906, Nr. 27.
5. Van Steenburg and Sommerville. Press Medicale, 1906, No. 24.
6. Rosenau and Andersen. Bull. Hyg. Lab., No. 23.
7. Pettit. Press Medicale, 1906, No. 82.
8. Vallee-Comp-rend-de l' Acad. des Sci., T. 142, No. 20.
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11. Roth-Schultz. Beitrag z. Klin der Tuberkulose, 1906, VI, 167.
12. Zeitschr. f. Tubercalose, March, 1907 (Roepke).
13. Wasserman and Bruck. Deutsch Med. Woch., 22 March, 1906, No. 12.
14. Citron. Berlin Klin. Woch., 1907, No. 36.
15. Trudeau. American Journal Med. Sci., June, 1907.

Discussion.

Dr. Hirschfelder: One of the most interesting facts in this paper was the resume of the report of the British Commission on Tuberculosis. I think they established the doctrine that Koch promulgated that bovine tuberculosis and human tuberculosis were distinct, and disproved his statement that bovine tuberculosis does not invade human beings. Koch appropriated the work of Theobald Smith without giving him credit for the pioneer work that he had done in differentiating the two bacilli so thoroughly. The Germans are divided into two sections, and followers of Koch still maintain that bovine tuberculosis does not occur in human beings while the larger group believe with the British commission. All of the cases in human beings are not due to the bovine, nor has it been clearly proven as yet that the human germ is a modified bovine. It is not impossible that the tuberculosis germ was originally the grass germ. It is not impossible that originally the cow became infected with a grass bacillus, and in passing through the cow the germ became modified and became adapted to life in the cow. The cow germ, in passing through the milk into the intestinal tract of the child or adult, produces that form of tuberculosis which the commission claims belongs to Class 1, which answers to the tests of the bovine tuberculosis. Gradually, during its numerous passages through the cow it may change to the form of the Class 3, and finally, in successive passages through the human body, may become the germ which is called the human germ. This is not at all impossible. However, I think it is very important that the report of this work of the British commission should be spread, and I think that the fear that the people will be too much frightened should hardly keep back this report any longer. I think the danger is that they will not be enough frightened.

WHEN IS GONORRHEA CURED?*

By JOHN C. SPENCER, M. D., San Francisco.

It is a simple answer to the question, "When is gonorrhea cured?" to say offhand, "When the gonococci have disappeared from, or are no longer demonstrable in the patient's secretions."

Upon this bald statement, however, depends a responsibility that is second to none in the entire realm of medicine; one that calls for the highest degree of patient and painstaking perseverance and diagnostic technic. So much depends on our dictum in the pronouncement of a final cure of this social curse, that the responsibility almost appalls.

If the proper education of the lay-public as to the seriousness of gonorrhea is to be brought about, it must surely be by the physician. Our moral weight is doubled by virtue of our dual position of father-confessor and medical adviser. Thus a judicious elucidation as to the nature and pathologic possibilities of gonorrhea, may be used to fit each individual's mental capacity, and emphasized from time to time.

The widespread fallacy among the ignorant, that the cessation of the urethral discharge means the termination of the disease, should be vigorously negatived.

Relatively it is this very complacency as to the disappearance of only the more striking of the objective symptoms, which is responsible for the

* Read at the Thirty-eighth annual meeting of the State Society, Coronado, April, 1908.